December 10, 2021

Norman Stockbridge, MD, Director
Division of Cardiovascular and Renal Products
Center for Drug Evaluation and Research
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

RE: Carospir® (Spironolactone Oral Suspension, 25 mg/5 mL)
NDA 209478, Sequence 0093
RESPONSE TO PREA NON-COMPLIANCE LETTER

Dear Dr. Stockbridge,

CMP Development LLC (CMP) submits today this response to the PREA Non-Compliance Letter dated 11/05/21 (Attachment 1) in reference to NDA 209478 for Carospir® (Spironolactone Oral Suspension, 25 mg/5 mL). Per NDA Approval Letter for NDA 209478 dated 08/04/2017 the following PREA post marketing requirements (PMR) were stated:

3256-1	Conduct a single-dose pharmakinetic study in pediatric patients 0 to < 17 years of age with edematous conditions.
3256-2	Conduct a multiple-dose pharmacokinetic, pharmacodynamics, and safety study in pediatric patients 0 to < 17 years of age with edematous conditions.

CMP submitted the first draft protocol for PREA PMR Study 3256-1 in August 2018 for the Agency review. Since then, through multiple communications, protocol revisions, FDA meetings, Advice Letters and Information Requests throughout 2019, 2020 and 2021 an agreement has been reached between CMP and the FDA for CMP to combine the two separate studies listed above into a single two-part study. A draft protocol for the single two-part study has already been submitted and reviewed by the Agency and revised multiple times over the past year. The most recent Advice Letter/Information Request dated 10/26/21 had further revisions requested to the combined study protocol. At this time CMP is revising the protocol to incorporate all of the FDA's most recent comments and CMP expects to submit this final version for review by the end of December 2021. Due to the multiple rounds of discussions, decision to change the strategy from two separate studies to a single combined study and multiple protocol revisions, CMP was not able to meet the Study 3256-1 final report deadline of August 2021.

Reference is made to email communication dated 11/12/21 (Attachment 2) from Christine Sadr, MS, Regulatory Health Project Manager, FDA indicating that the Agency acknowledges CMP's intention to combine the two studies into one study and the ongoing negotiations for the

replacement PMR to meet the PREA requirements. Additionally, this communication provided a suggested timeline for the replacement study as follows:

Final Protocol Submission: 01/2022
Study Completion: 01/2026
Final Report Submission: 01/2027

CMP agrees the proposed timeline is reasonable and in keeping with the original final deadline for the second study (3256-2). However, as CMP and CMP's clinical experts previously communicated in multiple responses and meetings, CMP anticipates significant enrollment issues due to the requirement for 24-hour urine collection in the older age groups and spot urine collection in infants and non-toilet trained patients. All efforts will be made to comply with this requirement but if/when enrollment issues begin to affect CMP's ability to meet the agreed timeline we agree to update the Agency in a timely manner.

In summary, CMP requests the following single combined study and proposed timeline replace the requirements for Studies 3256-1 and 3256-2 for NDA 209478 PREA PMRs.

Proposed Single Study: (b) (4)

Final Protocol Submission: 01/2022
Study Completion: 01/2026
Final Report Submission: 01/2027

CMP appreciates the Agency's feedback and advice throughout this process and look forward to revising our PREA PMRs to return to an "in compliance" status. Should you have any questions regarding this correspondence, you may contact me at 252-753-7111 or ellen.chrismon@cmppharma.com.

Sincerely,

Ellen Chrismon

Ellen Chrismon
Regulatory Affairs Manager
CMP Development LLC

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